PCT/EP2004/052262

Claims

1. Use of a compound of formula (I) for the manufacture of a medicament for the prevention or the treatment of HIV infection wherein the compound of formula (I) is a compound of formula

-91-

$$\begin{array}{c|c}
C & B \\
N & A
\end{array}$$
(1)

5

15

20

30

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof, wherein

A and B each represents a radical of formula

$$R^2$$
 (a) or X_1 R^3 (b) wherein

ring E represents phenyl, pyridyl, pyridazinyl, pyrimidinyl or pyrazinyl; ring F represents phenyl, pyridyl, pyridazinyl, pyrimidinyl or pyrazinyl; R¹ represents hydrogen; aryl; formyl; C₁-6alkylcarbonyl; C₁-6alkyloxycarbonyl;

C₁-6alkyl optionally substituted with formyl, C₁-6alkylcarbonyl,

C1-6alkyl optionally substituted with formyl, C1-6alkylcarbonyl,

 $\label{eq:constraint} C_{1\text{-}6alkyloxycarbonyl}, C_{1\text{-}6alkyloxycarbonyl}, or \ C_{1\text{-}6alkyloxycarbonyl}; or \ C_{1\text{-}6alkyloxycarbonyl};$

R² represents cyano; aminocarbonyl; mono- or di(C₁₋₄alkyl)aminocarbonyl; C₁₋₆alkyl optionally substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; C₂₋₆alkenyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; or C₂₋₆alkynyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl;

 X_1 represents $-NR^5$ -; -NH-NH-; -N=N-; -O-; -C(=O)-; $-C_{1-4}$ alkanediyl-; -CHOH-; -S-;

-S(=O) $_p$ -; -X2-C1-4alkanediyl-; -C1-4alkanediyl-X2-; or

 $-C_{1} -alkanediyl - X_2 - C_{1} -alkanediyl -;$

 X_2 represents -NR⁵-; -NH-NH-; -N=N-; -O-; -C(=O)-; -CHOH-; -S-; or -S(=O)_p-;

25 m represents an integer of value 1, 2, 3 or 4;

R³ represents cyano; aminocarbonyl; amino; halo; NHR¹³; NR¹³R¹⁴; -C(=O)-NHR¹³; -C(=O)-NR¹³R¹⁴; -C(=O)-R¹⁵; -CH=N-NH-C(=O)-R¹⁶; C₁-6alkyl optionally

substituted with one or more substituents each independently selected from R^{3a};

 C_{1-6} alkyloxy optionally substituted with one or more substituents each independently selected from R^{3a} ; C_{1-6} alkyloxy C_{1-6} alkyl optionally substituted with one or more substituents each independently selected from R^{3a} ; C_{2-6} alkenyl optionally substituted with one or more substituents each independently selected from R^{3a} ; C_{2-6} alkynyl

optionally substituted with one or more substituents each independently selected from R^{3a} ; $-C(=N-O-R^8)-C_{1-4}alkyl$; R^7 or $-X_3-R^7$;

$$\begin{split} R^{3a} \text{ represents halo, cyano, hydroxy, } NR^9R^{10}, -C(=O)-NR^9R^{10}, -C(=O)-C_{1\text{-}6}alkyl, \\ -C(=O)-O-C_{1\text{-}6}alkyl, -C(=O)-polyhaloC_{1\text{-}6}alkyl, -C(=O)-O-polyhaloC_{1\text{-}6}alkyl \text{ or } R^7; \end{split}$$

5 X_3 represents $-NR^5$ -; -NH-NH-; -N=N-; -O-; -C(=O)-; -S-; $-S(=O)_p$ -;

 $-X_{4a}-C_{1-4}$ alkanediyl-; $-C_{1-4}$ alkanediyl- X_{4b} -; $-C_{1-4}$ alkanediyl- $X_{4a}-C_{1-4}$ alkanediyl-; or $-C(=N-OR^8)-C_{1-4}$ alkanediyl-;

 X_{4a} represents $-NR^5$ -; -NH-NH-; -N=N-; -C(=O)-; -S-; or $-S(=O)_p$ -;

 X_{4b} represents -NH-NH-; -N=N-; -O-; -C(=O)-; -S-; or -S(=O)_p-;

- each R⁴ independently represents hydroxy; halo; C₁₋₆alkyl optionally substituted with one or more substituents each independently selected from R^{4a}; C₂₋₆alkenyl optionally substituted with one or more substituents each independently selected from R^{4a}; C₂₋₆alkynyl optionally substituted with one or more substituents each independently selected from R^{4a}; C₃₋₇cycloalkyl; C₁₋₆alkyloxy; C₁₋₆alkyloxycarbonyl;
- 15 C_{1-6} alkylcarbonyloxy; carboxyl; formyl; cyano; nitro; amino; mono- or $di(C_{1-6}$ alkyl)amino; polyhalo C_{1-6} alkyl; polyhalo C_{1-6} alkyloxy; polyhalo C_{1-6} alkylthio; $-S(=O)_pR^6$; $-NH-S(=O)_pR^6$; $-C(=O)R^6$; -NHC(=O)H; $-C(=O)NHNH_2$; $NHC(=O)R^6$; $-C(=NH)R^6$; or $-R^7$;

R^{4a} represents halo, cyano, NR⁹R¹⁰, hydroxy or -C(=O)R⁶;

- 20 R⁵ represents hydrogen; aryl; formyl; C₁₋₆alkylcarbonyl; C₁₋₆alkyloxycarbonyl; C₁₋₆alkyl optionally substituted with formyl, C₁₋₆alkylcarbonyl, C₁₋₆alkyloxycarbonyl or C₁₋₆alkylcarbonyloxy; or C₁₋₆alkyloxyC₁₋₆alkylcarbonyl substituted with C₁₋₆alkyloxycarbonyl;
 - R⁶ represents C₁₋₆alkyl, amino, mono- or di(C₁₋₄alkyl)amino or polyhaloC₁₋₄alkyl;
- 25 R⁷ represents a monocyclic, bicyclic or tricyclic saturated carbocycle; a monocyclic, bicyclic or tricyclic partially saturated carbocycle; a monocyclic, bicyclic or tricyclic aromatic carbocycle; a monocyclic, bicyclic or tricyclic partially saturated heterocycle; or a monocyclic, bicyclic or tricyclic partially saturated heterocycle; or a monocyclic, bicyclic or tricyclic aromatic heterocycle; wherein each of said carbocyclic or
- heterocyclic ring systems may, whenever possible, optionally be substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, mercapto, C₁-6alkyl, hydroxyC₁-6alkyl, aminoC₁-6alkyl, mono or di(C₁-6alkyl)aminoC₁-6alkyl, formyl, C₁-6alkylcarbonyl, C₃₋₇cycloalkyl, C₁-6alkyloxy, C₁-6alkyloxycarbonyl, C₁-6alkylthio, cyano, nitro,
- polyhaloC₁₋₆alkyl, polyhaloC₁₋₆alkyloxy, aminocarbonyl, -CH(=N-O-R⁸), R^{7a}, -X₃-R^{7a} or R^{7a}-C₁₋₄alkanediyl-;

-93-

```
R<sup>7a</sup> represents a monocyclic, bicyclic or tricyclic saturated carbocycle; a monocyclic,
           bicyclic or tricyclic partially saturated carbocycle; a monocyclic, bicyclic or tricyclic
           aromatic carbocycle; a monocyclic, bicyclic or tricyclic saturated heterocycle; a
           monocyclic, bicyclic or tricyclic partially saturated heterocycle; or a monocyclic,
 5
           bicyclic or tricyclic aromatic heterocycle; wherein each of said carbocyclic or
           heterocyclic ring systems may optionally be substituted with one, two, three, four or
           five substituents each independently selected from halo, hydroxy, mercapto,
           C1-6alkyl, hydroxyC1-6alkyl, aminoC1-6alkyl, mono or
           di(C<sub>1</sub>-6alkyl)aminoC<sub>1</sub>-6alkyl, formyl, C<sub>1</sub>-6alkylcarbonyl, C<sub>3-7</sub>cycloalkyl,
10
           C<sub>1</sub>-6alkyloxy, C<sub>1</sub>-6alkyloxycarbonyl, C<sub>1</sub>-6alkylthio, cyano, nitro,
           polyhaloC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyloxy, aminocarbonyl, -CH(=N-O-R<sup>8</sup>);
       R<sup>8</sup> represents hydrogen, C<sub>1,4</sub>alkyl optionally substituted with aryl, or aryl;
       R<sup>9</sup> and R<sup>10</sup> each independently represent hydrogen; hydroxy; C<sub>1-6</sub>alkyl; C<sub>1-6</sub>alkyloxy;
           C<sub>1-6</sub>alkylcarbonyl; C<sub>1-6</sub>alkyloxycarbonyl; amino; mono- or di(C<sub>1-6</sub>alkyl)amino;
15
           mono- or di(C<sub>1-6</sub>alkyl)aminocarbonyl; -CH(=NR<sup>11</sup>) or R<sup>7</sup>, wherein each of the
           aforementioned C<sub>1-6</sub>alkyl groups may optionally and each individually be substituted
           with one or two substituents each independently selected from hydroxy,
           C<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxycarbonyl, cyano, amino,
           imino, mono- or di(C<sub>1-4</sub>alkyl)amino, polyhaloC<sub>1-4</sub>alkyl, polyhaloC<sub>1-4</sub>alkyloxy,
           polyhaloC_{1-4}alkylthio, -S(=O)_{D}R^{6}, -NH-S(=O)_{D}R^{6}, -C(=O)R^{6}, -NHC(=O)H,
20
           -C(=O)NHNH<sub>2</sub>, -NHC(=O)\mathbb{R}^6, -C(=NH)\mathbb{R}^6, or \mathbb{R}^7; or
       R<sup>9</sup> and R<sup>10</sup> may be taken together to form a bivalent or trivalent radical of formula
                  -CH2-CH2-CH2-CH2-
                                                                   (d-1);
                  -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-
                                                                   (d-2);
25
                  -CH2-CH2-O-CH2-CH2-
                                                                  (d-3);
                  -CH2-CH2-S-CH2-CH2-
                                                                  (d-4);
                  -CH<sub>2</sub>-CH<sub>2</sub>-NR<sup>12</sup>-CH<sub>2</sub>-CH<sub>2</sub>-
                                                                  (d-5);
```

R¹¹ represents cyano; C₁₋₄alkyl optionally substituted with C₁₋₄alkyloxy, cyano, amino, mono- or di(C₁₋₄alkyl)amino or aminocarbonyl; C₁₋₄alkylcarbonyl;

C₁₋₄alkyloxycarbonyl; aminocarbonyl; mono- or di(C₁₋₄alkyl)aminocarbonyl;

(d-6); or

(d-7);

R¹² represents hydrogen or C₁₋₄alkyl;

-CH2-CH=CH-CH2-

=CH-CH=CH-CH=CH-

R¹³ and R¹⁴ each independently represent C₁₋₆alkyl optionally substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; C₂₋₆alkenyl optionally substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl;

WO 2005/028479

-94-

PCT/EP2004/052262

 C_{2-6} alkynyl optionally substituted with cyano, aminocarbonyl or mono- or di(C_{1-4} alkyl)aminocarbonyl;

R¹⁵ represents C₁₋₆alkyl optionally substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl;

- 5 R¹⁶ represents C₁₋₆alkyl optionally substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; or R⁷;
 - -C-D- represents a bivalent radical of formula

-N=CH-NR¹⁷-

(c-1); or

-NR¹⁷-CH=N-

15

(c-2);

- 10 R¹⁷ represents hydrogen; C₁₋₆alkyl optionally substituted with hydroxy, cyano, aminocarbonyl, mono-or di(C₁₋₄alkyl)aminocarbonyl, C₁₋₄alkyloxycarbonyl or aryl; p represents an integer of value 1 or 2;
 - aryl represents phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, hydroxy, mercapto, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, aminoC₁₋₆alkyl, mono or di(C₁₋₆alkyl)aminoC₁₋₆alkyl,

 C_{1-6} alkylcarbonyl, C_{3-7} cycloalkyl, C_{1-6} alkyloxy, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylthio, cyano, nitro, polyhalo C_{1-6} alkyl, polyhalo C_{1-6} alkyloxy, aminocarbonyl, R^7 or $-X_3-R^7$;

provided that when A represents a radical of formula (a) then B represents a radical of formula (b) and when A represents a radical of formula (b) then B represents a radical of formula (a).

- A compound as defined in claim 1 provided that when R² represents aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl then R³ represents cyano; -C(=O)-R¹5;
 -CH=N-NH-C(=O)-R¹6; C₁-6alkyl substituted with one or more substituents each independently selected from R³b; C₁₋₆alkyloxy substituted with one or more substituents each independently selected from R³a; C₁₋₆alkyloxyC₁₋₆alkyl optionally substituted with one or more substituents each independently selected from R³a;
 C₂-6alkenyl optionally substituted with one or more substituents each independently selected from R³a; C₂-6alkynyl optionally substituted with one or more substituents each independently selected from R³a; -C(=N-O-R³)-C₁₋₄alkyl; R² or -X₃-R²; with R³b representing cyano, hydroxy, NR³R¹o, -C(=O)-NR³R¹o, -C(=O)-C₁₋₆alkyl, -C(=O)-polyhaloC₁₋₆alkyl, -C(=O)-O-polyhaloC₁₋₆alkyl or R².
- 35 3. A compound according to claim 2 wherein the compound has the formula

WO 2005/028479 PCT/EP2004/052262

-95-

PCT/EP2004/052262

$$(R^4)_m$$
 F
 R^3
 $(I-A)$

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof,

wherein R¹, R², R³, R⁴, ring E, ring F, C, D and m are as defined in claim 1.

4. A compound according to claim 3 wherein the compound of formula (I-A) has the formula

$$R^4$$
 R^4
 R^3
 R^4
 R^4

5

10

20

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof,

wherein R¹, R², R³, R⁴, ring E, ring F, C and D are as defined in claim 1.

5. A compound according to claim 2 wherein the compound has the formula

$$\begin{array}{c|c}
R^{1} & E \\
\hline
R^{2} \\
N & (R^{4})_{m} \\
\hline
R^{3}
\end{array}$$
(I-B)

a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof,

wherein R¹, R², R³, R⁴, ring E, ring F, C, D and m are as defined in claim 1.

6. A compound according to claim 5 wherein the compound of formula (I-B) has the formula

PCT/EP2004/052262

$$R^{1}$$
 E
 R^{2}
 R^{2}
 R^{4}
 R^{4}
 R^{4}
 R^{3}
 R^{4}
 R^{4}

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof,

-96-

wherein R¹, R², R³, R⁴, ring E, ring F, C and D are as defined in claim 1.

5

20

- 7. A compound according to any one of claims 2 to 6 wherein ring E is phenyl.
- 8. A compound according to any one of claims 2 to 7 wherein ring F is phenyl.
- 10 9. A compound according to claim 2 wherein the compound has the formula

$$(R^{4})_{m} = \begin{pmatrix} R^{3} \\ b^{1} \\ b^{2} \\ b^{2} \\ b^{2} \\ k_{1} \\ k_{1} \\ k_{2} \\ k_{3} \\ k_{4} \\ k_{1} \\ k_{1} \\ k_{2} \\ k_{3} \\ k_{4} \\ k_{1} \\ k_{2} \\ k_{3} \\ k_{4} \\ k_{3} \\ k_{4} \\ k_{3} \\ k_{4} \\ k_{3} \\ k_{4} \\ k_{4} \\ k_{3} \\ k_{4} \\ k_{5} \\ k_{5} \\ k_{6} \\ k_{6$$

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof, wherein

 $-a^1=a^2-C(R^2)=a^3-a^4=$ represents a bivalent radical of formula

15 -CH=CH-C(
$$\mathbb{R}^2$$
)=CH-CH= (a-1);

$$-N=CH-C(R^2)=CH-CH=$$
 (a-2);

$$-CH=N-C(R^2)=CH-CH=$$
 (a-3);

$$-N=CH-C(R^2)=N-CH=$$
 (a-4);

$$-N=CH-C(R^2)=CH-N=$$
 (a-5);

-CH=N-C(
$$R^2$$
)=N-CH= (a-6); or

$$-N=N-C(R^2)=CH-CH=$$
 (a-7);

-b¹=b²-b³=b⁴- represents a bivalent radical of formula

(b-2);

WO 2005/028479 PCT/EP2004/052262

-97-

PCT/EP2004/052262

-N=CH-N=CH-(b-3);-N=CH-CH=N-(b-4); or -N=N-CH=CH-(b-5);-C-D- represents a bivalent radical of formula -N=CH-NR17-5 (c-1); or -NR¹⁷-CH=N-(c-2);m represents an integer of value 1, 2, 3 and in case $-b^1=b^2-b^3=b^4$ is (b-1), then m may also be 4: R¹ represents hydrogen; aryl; formyl; C₁₋₆alkylcarbonyl; C₁₋₆alkyloxycarbonyl; 10 C₁-6alkyl optionally substituted with formyl, C₁-6alkylcarbonyl, C₁-6alkyloxycarbonyl, C₁-6alkylcarbonyloxy; or C₁-6alkyloxyC₁-6alkylcarbonyl substituted with C₁₋₆alkyloxycarbonyl; R² represents cyano; aminocarbonyl; mono- or di(C₁₋₄alkyl)aminocarbonyl; C₁₋₆alkyl optionally substituted with cyano, aminocarbonyl or mono- or 15 di(C₁₋₄alkyl)aminocarbonyl; C₂₋₆alkenyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; or C₂₋₆alkynyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; X₁ represents –NR⁵-, -NH-NH-, -N=N-, -O-, -C(=O)-, C₁₋₄alkanediyl, -CHOH-, -S-, - $S(=O)_{p}$, $-X_2$ - C_{1-4} alkanediyl- or $-C_{1-4}$ alkanediyl- X_2 -; 20 X_2 represents $-NR^5$ -, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)_n-; R³ represents NHR¹³; NR¹³R¹⁴; -C(=O)-NHR¹³; -C(=O)-NR¹³R¹⁴; -C(=O)-R¹⁵; -CH=N-NH-C(=O)-R¹⁶; cyano; halo; C₁-6alkyl; polyhaloC₁-6alkyl; C₁-6alkyl substituted with one or more substituents each independently selected from cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C₁₋₆alkyl substituted with hydroxy and a second substituent selected from cyano, NR⁹R¹⁰, -C(=0)-25 $NR^9R^{10}, -C(=O)-C_{1-6} \\ alkyl \ or \ R^7; \ C_{1-6} \\ alkyloxyC_{1-6} \\ alkyl \ optionally \ substituted \ with$ one or more substituents each independently selected from cyano, NR⁹R¹⁰. -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C₁₋₆alkyloxy optionally substituted with one or more substituents each independently selected from cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C₂₋₆alkenyl optionally substituted with 30 one or more substituents each independently selected from halo, cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C₂₋₆alkynyl optionally substituted with one or more substituents each independently selected from halo, cyano, NR⁹R¹⁰, $-C(=O)-NR^9R^{10}$, $-C(=O)-C_{1-6}$ alkyl or R^7 ; $-C(=N-O-R^8)-C_{1-4}$ alkyl; R^7 or $-X_3-R^7$; X_3 is $-NR^5$ -, -NH-NH-, -N=N-, -O-, -C(=O)-, -S-, -S(=O)_n-, $-X_{4b}$ - $-C_{1-4}$ alkanediyl-, 35

-C₁₋₄alkanediyl-X_{4a}-, -C₁₋₄alkanediyl-X_{4b}-C₁₋₄alkanediyl,

-C(=N-OR⁸)-C₁₋₄alkanediyl-;

5

10

15

25

35

with X_{4a} being -NH-NH-, -N=N-, -O-, -C(=O)-, -S-, -S(=O)_p-; and with X_{4b} being -NH-NH-, -N=N-, -C(=O)-, -S-, -S(=O)_p-; each R⁴ independently represents halo, hydroxy, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyl, aminoC₁₋₆alkyl, cyano, nitro, polyhaloC₁₋₆alkyl, polyhaloC₁₋₆alkyloxy, aminocarbonyl, mono- or di(C₁₋₄alkyl)aminocarbonyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkylcarbonyl, formyl, amino, mono- or di(C₁₋₄alkyl)amino or R⁷:

R⁵ is hydrogen; aryl; formyl; C₁-6alkylcarbonyl; C₁-6alkyloxycarbonyl; C₁-6alkyl optionally substituted with formyl, C₁-6alkylcarbonyl, C₁-6alkylcarbonyl or C₁-6alkylcarbonyloxy; or C₁-6alkyloxyC₁-6alkylcarbonyl substituted with C₁-6alkyloxycarbonyl;

 R^6 is C_{1-4} alkyl, amino, mono- or di $(C_{1-4}$ alkyl)amino or polyhalo C_{1-4} alkyl;

- R⁷ is a monocyclic, bicyclic or tricyclic saturated, partially saturated or aromatic carbocycle or a monocyclic, bicyclic or tricyclic saturated, partially saturated or aromatic heterocycle, wherein each of said carbocyclic or heterocyclic ring systems may optionally be substituted where possible with one, two, three, four or five substituents each independently selected from halo, hydroxy, mercapto, C₁-6alkyl, hydroxyC₁-6alkyl, aminoC₁-6alkyl, mono or di(C₁-6alkyl)aminoC₁-6alkyl, formyl, C₁-6alkylcarbonyl, C₃₋₇cycloalkyl, C₁-6alkyloxy, C₁-6alkyloxycarbonyl,
- 20 C₁₋₆alkylthio, cyano, nitro, polyhaloC₁₋₆alkyl, polyhaloC₁₋₆alkyloxy, aminocarbonyl, -CH(=N-O-R⁸), R^{7a}, -X₃-R^{7a} or R^{7a}-C₁₋₄alkanediyl-;
 - R^{7a} is a monocyclic, bicyclic or tricyclic saturated, partially saturated or aromatic carbocycle or a monocyclic, bicyclic or tricyclic saturated, partially saturated or aromatic heterocycle, wherein each of said carbocyclic or heterocyclic ring systems may optionally be substituted where possible with one, two, three, four or five substituents each independently selected from halo, hydroxy, mercapto, C₁-6alkyl, hydroxyC₁-6alkyl, aminoC₁-6alkyl, mono or di(C₁-6alkyl)aminoC₁-6alkyl, formyl, C₁-6alkylcarbonyl, C₃₋₇cycloalkyl, C₁-6alkyloxy, C₁-6alkyloxy, C₁-6alkyloxy, C₁-6alkyloxy,

aminocarbonyl, or -CH(=N-O-R⁸);

- R⁸ is hydrogen, C₁₋₄alkyl optionally substituted with aryl, or aryl;
- R⁹ and R¹⁰ each independently are hydrogen; C₁₋₆alkyl; C₁₋₆alkylcarbonyl; C₁₋₆alkyloxycarbonyl; amino; mono- or di(C₁₋₆alkyl)amino; mono- or di(C₁₋₆alkyl)aminocarbonyl; -CH(=NR¹¹) or R⁷, wherein each of the aforementioned C₁₋₆alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, hydroxyC₁₋₆alkyloxy, carboxyl, C₁₋₆alkyloxycarbonyl, cyano, amino, imino, mono-

```
or di(C<sub>1</sub>-4alkyl)amino, polyhaloC<sub>1-4</sub>alkyl, polyhaloC<sub>1-4</sub>alkyloxy,
            polyhaloC_{1-4}alkylthio, -S(=O)_{D}R^{6}, -NH-S(=O)_{D}R^{6}, -C(=O)R^{6}, -NHC(=O)H,
           -C(=O)NHNH_2, -NHC(=O)R^6, -C(=NH)R^6, R^7; or
       R<sup>9</sup> and R<sup>10</sup> may be taken together to form a bivalent or trivalent radical of formula
 5
                    -CH2-CH2-CH2-CH2-
                                                                       (d-1);
                    -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-
                                                                       (d-2);
                    -CH2-CH2-O-CH2-CH2-
                                                                       (d-3);
                    -CH2-CH2-S-CH2-CH2-
                                                                       (d-4);
                    -CH<sub>2</sub>-CH<sub>2</sub>-NR<sup>12</sup>-CH<sub>2</sub>-CH<sub>2</sub>-
                                                                      (d-5);
10
                    -CH2-CH=CH-CH2-
                                                                      (d-6); or
                   =CH-CH=CH-CH=CH-
                                                                      (d-7);
       R^{11} represents cyano; C_{1\text{--}4} alkyl optionally substituted with C_{1\text{--}4} alkyloxy, cyano, amino,
            mono- or di(C<sub>1-4</sub>alkyl)amino or aminocarbonyl; C<sub>1-4</sub>alkylcarbonyl;
            C<sub>1-4</sub>alkyloxycarbonyl; aminocarbonyl; mono- or di(C<sub>1-4</sub>alkyl)aminocarbonyl;
        R<sup>12</sup> represents hydrogen or C<sub>1-4</sub>alkyl;
15
       R<sup>13</sup> and R<sup>14</sup> each independently represent C<sub>1-6</sub>alkyl optionally substituted with cyano,
            aminocarbonyl or mono- or di(C<sub>1-4</sub>alkyl)aminocarbonyl; C<sub>2-6</sub>alkenyl optionally
            substituted with cyano, aminocarbonyl or mono- or di(C<sub>1-4</sub>alkyl)aminocarbonyl;
            C<sub>2-6</sub>alkynyl optionally substituted with cyano, aminocarbonyl or mono- or
20
            di(C<sub>1-4</sub>alkyl)aminocarbonyl;
        R<sup>15</sup> represents C<sub>1-6</sub>alkyl substituted with cyano, aminocarbonyl or mono- or
            di(C<sub>1-4</sub>alkyl)aminocarbonyl;
        R<sup>16</sup> represents C<sub>1-6</sub>alkyl optionally substituted with cyano, aminocarbonyl or mono- or
            di(C<sub>1-4</sub>alkyl)aminocarbonyl; or R<sup>7</sup>;
       R<sup>17</sup> represents hydrogen; C<sub>1.6</sub>alkyl; or C<sub>1.6</sub>alkyl substituted with aryl;
25
       p is 1 or 2;
        aryl represents phenyl or phenyl substituted with one, two, three, four or five
            substituents each independently selected from halo, hydroxy, mercapto, C<sub>1-6</sub>alkyl,
           hydroxyC<sub>1</sub>-6alkyl, aminoC<sub>1</sub>-6alkyl, mono or di(C<sub>1</sub>-6alkyl)aminoC<sub>1</sub>-6alkyl,
30
           C<sub>1</sub>-6alkylcarbonyl, C<sub>3-7</sub>cycloalkyl, C<sub>1</sub>-6alkyloxy, C<sub>1</sub>-6alkyloxycarbonyl,
           C<sub>1</sub>-6alkylthio, cyano, nitro, polyhaloC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyloxy,
           aminocarbonyl, R<sup>7</sup> or -X<sub>3</sub>-R<sup>7</sup>;
       provided that when R<sup>2</sup> represents aminocarbonyl or mono- or
        di(C<sub>1-4</sub>alkyl)aminocarbonyl then R<sup>3</sup> represents -C(=O)-R<sup>15</sup>; -CH=N-NH-C(=O)-R<sup>16</sup>;
35
       cyano; C1-6alkyl substituted with one or more substituents each independently selected
       from cyano, NR<sup>9</sup>R<sup>10</sup>, -C(=O)-NR<sup>9</sup>R<sup>10</sup>, -C(=O)-C<sub>1-6</sub>alkyl or R<sup>7</sup>; C<sub>1-6</sub>alkyl substituted
       with hydroxy and a second substituent selected from cyano, NR<sup>9</sup>R<sup>10</sup>, -C(=0)-NR<sup>9</sup>R<sup>10</sup>,
```

WO 2005/028479 PCT/EP2004/052262

-C(=O)-C₁₋₆alkyl or R⁷; C_{1-6} alkyloxy C_{1-6} alkyl optionally substituted with one or more substituents each independently selected from cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C_{1-6} alkyloxy substituted with one or more substituents each independently selected from cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C_{2-6} alkenyl optionally substituted with one or more substituents each independently selected from halo, cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; C_{2-6} alkynyl optionally substituted with one or more substituents each independently selected from halo, cyano, NR⁹R¹⁰, -C(=O)-NR⁹R¹⁰, -C(=O)-C₁₋₆alkyl or R⁷; $-C(=N-O-R^8)-C_{1-4}$ alkyl; R⁷ or $-X_3-R^7$.

10

15

- 10. A compound according to any one of claims 2 to 9 wherein R² represents cyano; aminocarbonyl; mono- or di(C₁₋₄alkyl)aminocarbonyl; C₁₋₆alkyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; C₂₋₆alkenyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl; or C₂₋₆alkynyl substituted with cyano, aminocarbonyl or mono- or di(C₁₋₄alkyl)aminocarbonyl.
- 11. A compound according to any one of claims 2 to 10 wherein R² represents cyano or aminocarbonyl.

20

12. A compound according to any one of claims 2 to 11 wherein R³ is cyano; aminocarbonyl; C₁₋₆alkyl optionally substituted with cyano or aminocarbonyl; C₁₋₆alkyloxy optionally substituted with cyano or aminocarbonyl; C₂₋₆alkenyl substituted with cyano or aminocarbonyl.

25

30

35

- 13. A compound according to any one of claims 2 to 9 wherein m is 2; R¹ represents hydrogen; R² represents cyano, aminocarbonyl or C₁₋₆alkyl; R³ represents cyano; C₁₋₆alkyl; C₁₋₆alkyl substituted with cyano; C₁₋₆alkyloxy optionally substituted with cyano; C₂₋₆alkenyl substituted with cyano or -C(=O)-NR⁹R¹⁰; each R⁴ independently represents halo, C₁₋₆alkyl or C₁₋₆alkyloxy; X₁ represents –NR⁵- or -O-; R⁵ represents hydrogen; R⁹ and R¹⁰ each independently are hydrogen or C₁₋₆alkyl; or R⁹ and R¹⁰ may be taken together to form a bivalent radical of formula -CH₂-CH₂-O-CH₂-(d-3); R¹⁷ is hydrogen; C₁₋₆alkyl optionally substituted with hydroxy, cyano, aminocarbonyl, C₁₋₄alkyloxycarbonyl or aryl; aryl is phenyl substituted with C₁₋₆alkyloxy.
- 14. A compound according to claim 2 wherein the compound is selected from

a N-oxide, a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof.

- 5 15. A compound according to any one of claims 2 to 14 for use as a medicine.
 - 16 A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 2 to 14.

10

17. A process for preparing a pharmaceutical composition according to claim 16 characterized in that a therapeutically effective amount of a compound as claimed in any one of claims 2 to 14 is intimately mixed with a pharmaceutically acceptable carrier.

15

20

(II-b)

18. A process for preparing a compound as claimed in claim 2, characterized by a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III) in the presence of a suitable catalyst, a suitable ligand, a suitable base, and a suitable solvent,

5

10

with W_1 representing a suitable leaving group, R^{17b} representing C_{1-6} alkyl optionally substituted with aryl, and A and B being defined as in claim 2; b) reacting an intermediate of formula (II'-a) or (II'-b) with an intermediate of formula (III') in the presence of a suitable catalyst, a suitable ligand, a suitable base, and a suitable solvent,

with W_1 representing a suitable leaving group, R^{17b} representing C_{1-6} alkyl optionally substituted with aryl, and A and B being defined as in claim 2; c) by converting a compound of formula (I-a) or (I-b) into a compound of formula (I-c) and (I-d) by reaction with a suitable acid,

with R^{17b} representing C_{1-6} alkyl optionally substituted with aryl, and A and B being defined as in claim 2;

10

d) converting a compound of formula (I-c) into a compound of formula (I-e) by reaction with an intermediate of formula R^{17c} - W_2 in the presence of a suitable base and a suitable solvent,

with W_2 representing a suitable leaving group, R^{17c} representing C_{1-6} alkyl optionally substituted with cyano or C_{1-4} alkyloxycarbonyl, and A and B being defined as in claim 2;

e) converting a compound of formula (I-e-1) into a compound of formula (I-f), by reaction with NH₃ in the presence of a suitable solvent,

with A and B being defined as in claim 2;

f) converting a compound of formula (I-e-1) into a compound of formula (I-g), by reaction with NaBH₄ in the presence of a suitable solvent,

with A and B being defined as in claim 2;

g) converting a compound of formula (I-f) into a compound of formula (I-h), by reaction with POCl₃ in the presence of a suitable solvent,

-106-

PCT/EP2004/052262

with A and B being defined as in claim 2;

or, if desired, further converting compounds of formula (I) into each other following art-known transformations; or further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or conversely, converting the acid addition salt form into the free base by treatment with alkali; or, if desired, preparing stereochemically isomeric forms, N-oxide forms or quaternary amines thereof.

10

5

- 19. A product containing (a) a compound as defined in any one of claims 1 to 14, and (b) another antiretroviral compound, as a combined preparation for simultaneous, separate or sequential use in the treatment of HIV infection.
- 20. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredients (a) a compound as defined in any one of claims 1 to 14, and (b) another antiretroviral compound.